

Radiologic Findings of Various Disorders Related to Chemotherapy in Children¹

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Because available therapy cannot always distinguish between malignant and nonmalignant cells, the toxicity of chemotherapeutic agents to normal tissue remains a troublesome issue. Various chemotherapeutic agents such as bleomycin, doxorubicin, cyclophosphamide and L-asparaginase, which cause pulmonary fibrosis, cardiomyopathy, pancreatitis, and hemorrhagic cystitis, respectively, are familiar to radiologists. The purpose of this report is to describe the radiologic findings of various organ abnormalities related to chemotherapy.

Index words : Radiography, in infants and children
Chemotherapy

Unfortunately, most effective treatments used in cancer chemotherapy have a narrow therapeutic index, and so acute and chronic toxicity is inevitable(1). The short- or long-term use of chemotherapeutic agents leads to various organ abnormalities; these are caused either by toxicity of the drug itself (cardiomyopathy, pulmonary fibrosis, pancreatitis, hemorrhagic cystitis, and neurotoxicity) or by immunosuppression (opportunistic infection). In order to increase familiarity with various organ disorders which follow cancer chemotherapy, and thus to increase diagnostic accuracy, we describe the radiologic findings of such disorders.

Cardiomyopathy

Anthracycline includes the anticancer agents doxorubicin (Adriamycin) and daunorubicin, which are commonly used in pediatric oncologic patients. Conventional doses of anthracycline often lead to permanent myocardial damage(2). The drug causes early cardiomyopathy or pericarditis as well as late-onset ventricular dysfunction even years after treatment has

ceased. Left ventricular ejection fraction, as seen on echocardiography, is routinely used to screen for anthracycline-induced cardiotoxicity. Chest radiographs may show cardiomegaly due to pericardial effusion or dilated cardiomyopathy(Fig. 1).

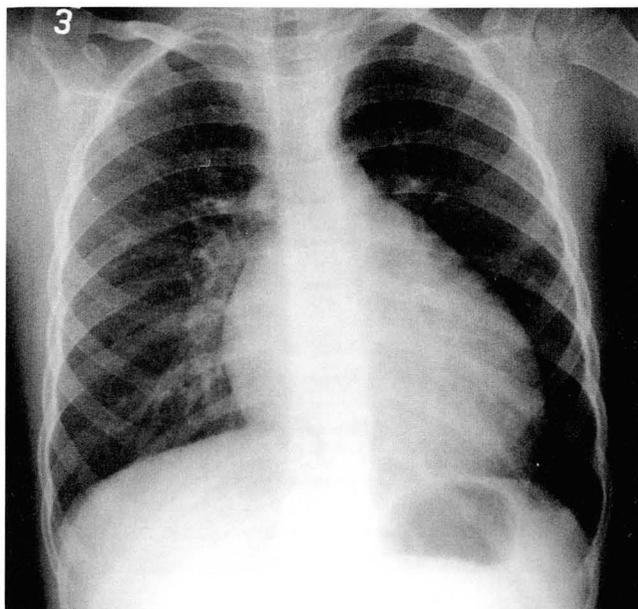


Fig. 1. Adriamycin-induced dilated cardiomyopathy. A 4 year-old girl with acute myeloid leukemia was treated with daunomycin and cytarabine. Plain chest radiograph shows moderate to severe cardiomegaly which is consistent with dilated cardiomyopathy.

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Pulmonary Toxicity

The important pulmonary side effects of bleomycin are well known, and interstitial lung disease develops in approximately 10% of patients treated with this drug(3). The pulmonary effects of bleomycin are dose dependent and a maximum cumulative dose of 250mg/m² is recommended. Pneumonitis occurs initially, and as in all cases of interstitial pulmonary fibrosis, this is followed by the accumulation of fibroblasts and collagen fibers. Thin-section CT offers the best spatial and contrast resolution ; peripheral ground-glass opacities, reticular densities, and fibrosis are demonstrated(Fig. 2).

Pancreatitis

Acute pancreatitis is an uncommon but serious complication of cancer chemotherapy ; it may be caused by chemotherapeutic agents such as L-asparaginase and 6-mercaptopurine(4). Abdominal imaging including US and CT is needed to diagnose and monitor this condition(Fig. 3).

Hemorrhagic Cystitis

The major side-effects of the alkylating agents such as cyclophosphamide and ifosfamide are nausea and vomiting, bone marrow suppression, sterility, alopecia, hemorrhagic cystitis, and urothelial carcinoma

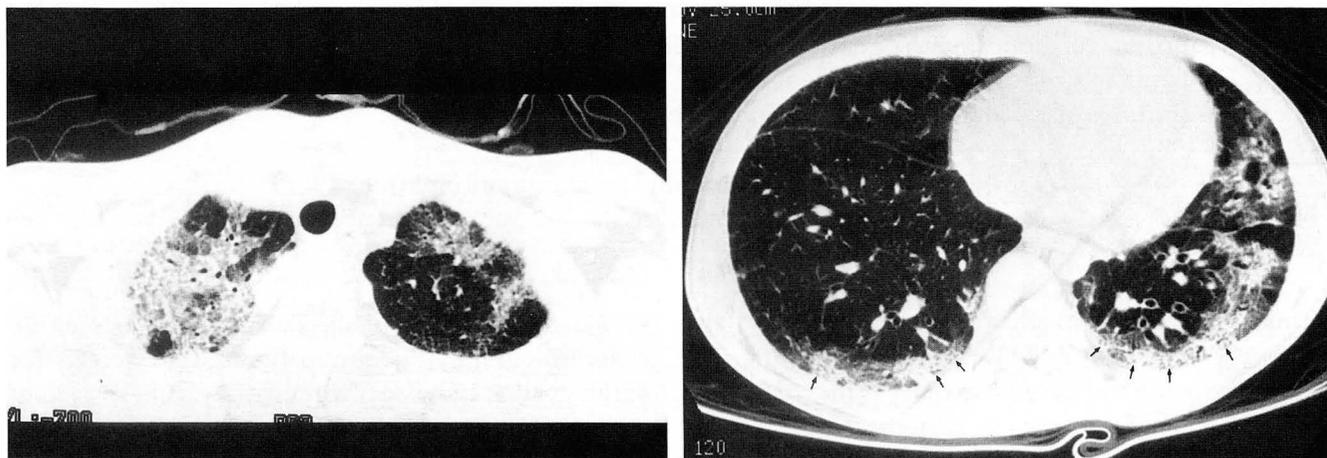


Fig. 2. Bleomycin-induced pulmonary fibrosis. An 11 year-old girl developed severe dyspnea while undergoing chemotherapy with a regimen including bleomycin for ovarian endodermal sinus tumor. **A.** and **B.** Thin-section CT scan reveals areas of ground-glass opacities with peripheral subpleural distribution. Fine honeycombing (arrows) with septal lines are also noted.

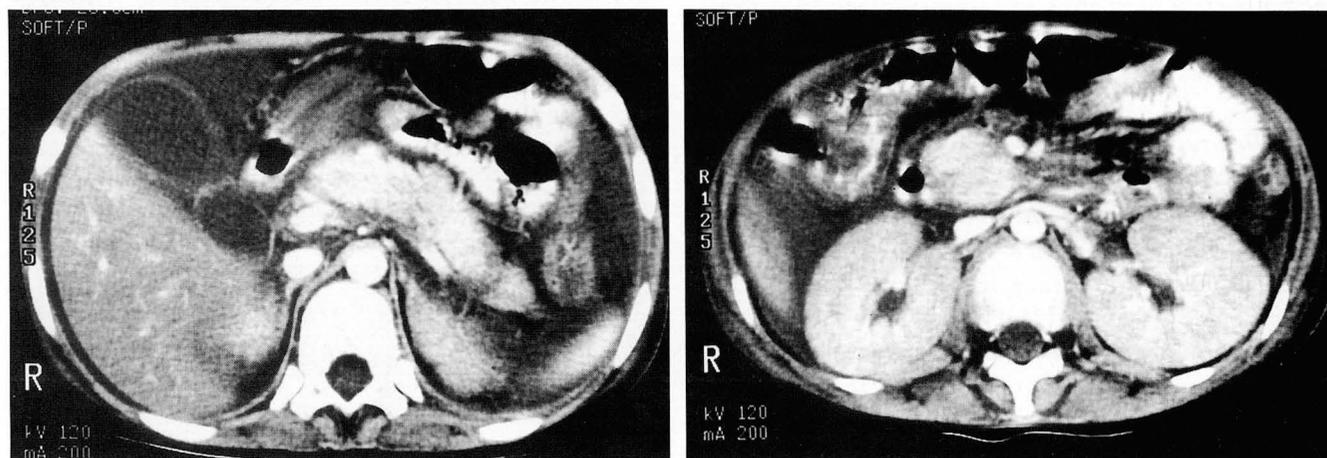


Fig. 3. Pancreatitis secondary to L-asparaginase. An 8 year-old boy with acute lymphoblastic leukemia was suffering from epigastric pain during the chemotherapy. Serum amylase was elevated up to 1105u/l. **A.** Postcontrast CT scan reveals diffuse swelling of the pancreas with intense enhancement and a large amount of ascites. **B.** Both kidneys show globular swelling and poor contrast enhancement with no contrast excretion into the collecting system indicating acute renal failure.

(5). Hydration and the use of mesna (antagonist of a toxic product) may reduce the occurrence of cystitis. US and MR show thickened and lobulated bladder mucosa(Fig. 4).

Hepatic Injury

Most chemotherapeutic agents used in cases of

childhood tumors exert hepatotoxic effects (6); diffuse fatty change and zonal necrosis are especially common. Cholestasis, hepatic veno-occlusive disease, hepatitis, fibrosis and cirrhosis may occur. Corticosteroids, methotrexate, 6-mercaptopurine, and L-asparaginase can cause fatty change (6); a fatty liver, for example, may be demonstrated by US and CT(Fig. 5).

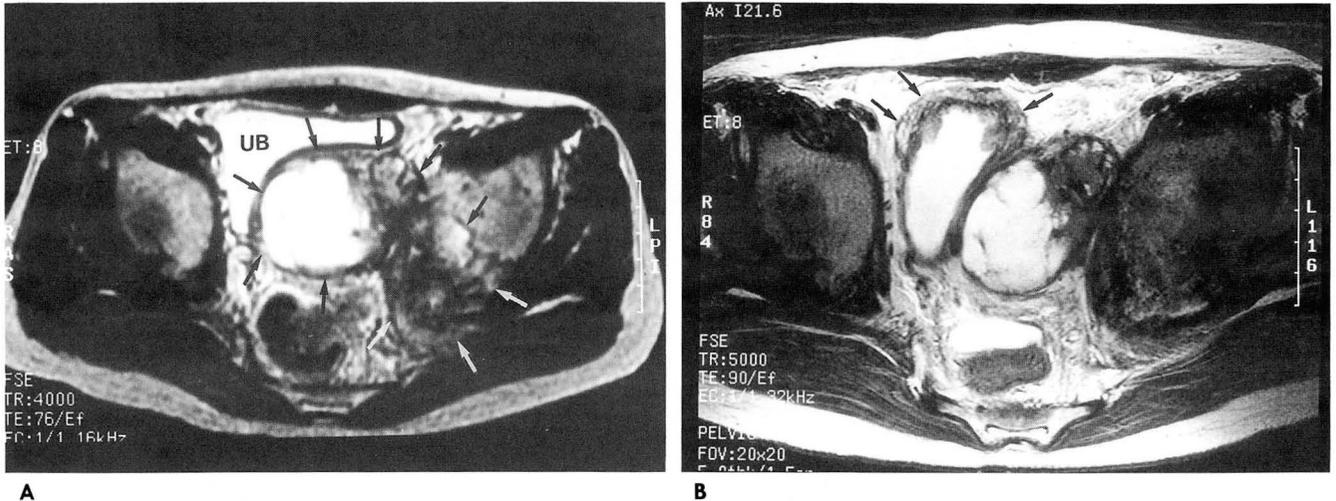


Fig. 4. Ifosfamide-induced hemorrhagic cystitis. A 14 year-old boy with Ewing sarcoma of the left ischium was treated with ifosfamide.

A. Initial MR T2-weighted image shows a large irregular mass involving left ischium, extending to the pelvic cavity(arrows). Most of the pelvic part of the tumor shows hyperintensity due to tumor necrosis. Note displaced but otherwise normal bladder(UB).

B. Three months later, he developed hematuria, dysuria, and urinary frequency. Follow-up MR T2-weighted image shows thickened and lobulated bladder wall(arrows). Again seen is the pelvic mass without significant interval change in its extent.

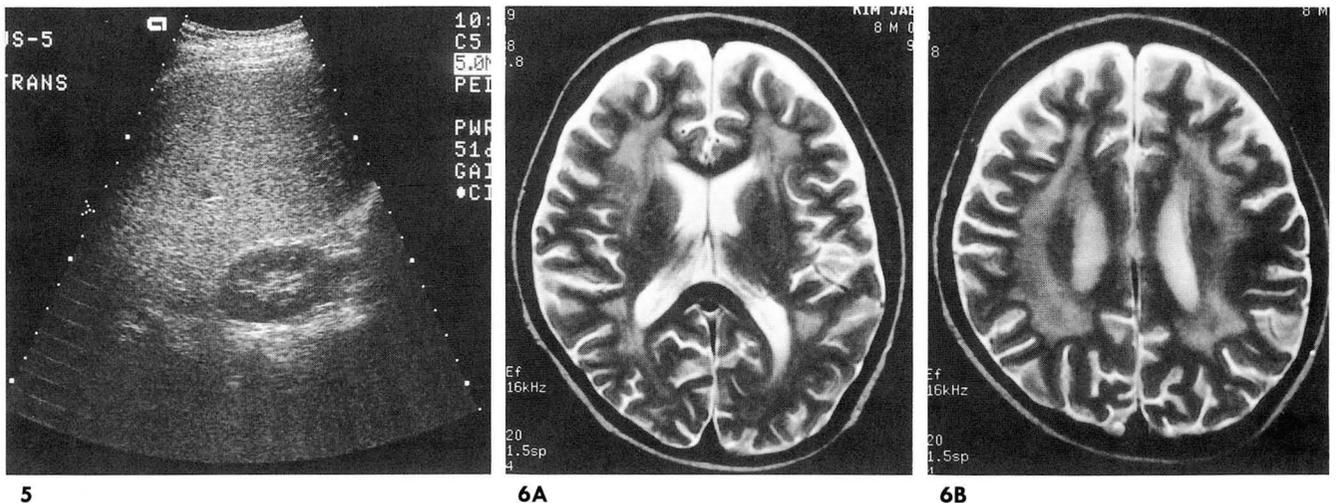


Fig. 5. Chemotherapy-induced fatty liver. An 11 year-old boy with acute lymphoblastic lymphoma received chemotherapy with prednisone and methotrexate. Three months later, transaminase level was elevated. Ultrasonography shows diffusely increased echogenicity of the liver as compared to the right kidney, which suggests fatty liver. Biopsy confirmed fatty infiltration in the liver.

Fig. 6. Leukoencephalopathy due to intrathecal methotrexate in a same patient to Fig. 3.

A and B. Axial T2-weighted MR images show bilaterally symmetric and confluent high signal intensities in the periventricular white matter. Note sparing of the subcortical arcuate fibers.

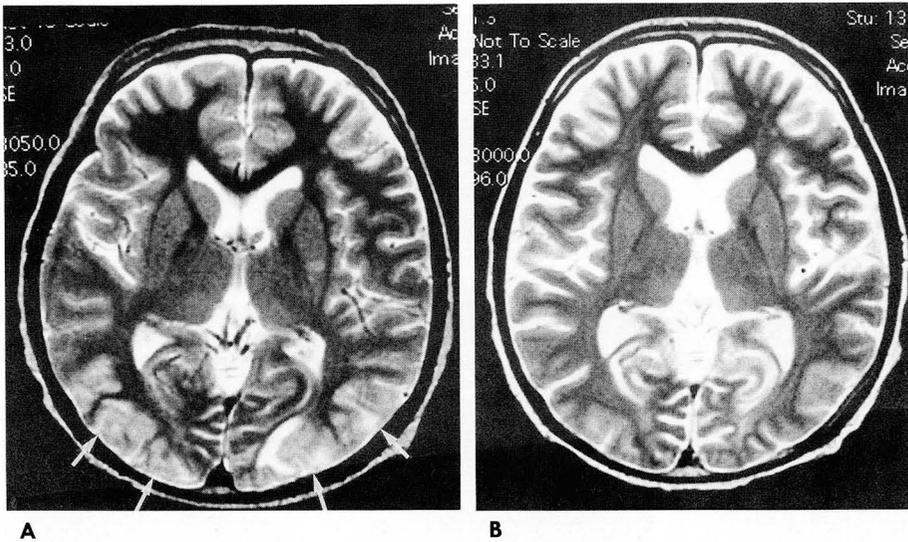


Fig. 7. Cyclosporine-induced hypertensive encephalopathy. A 15 year-old girl with aplastic anemia developed vomiting and seizure 10 days after bone marrow transplantation. Her blood pressure was 150/100mm Hg for three days.

A. Axial T2-weighted image shows high signal intensities involving the cortex and subcortical white matter in the parietooccipital regions(arrow-s).

B. Follow-up T2-weighted MR imaging after discontinuation of cyclosporine for two weeks. High signal intensities in the cortex and subcortical white matter have resolved. There is some residual hyperintensity in the white matter, with mild ventricular dilatation.

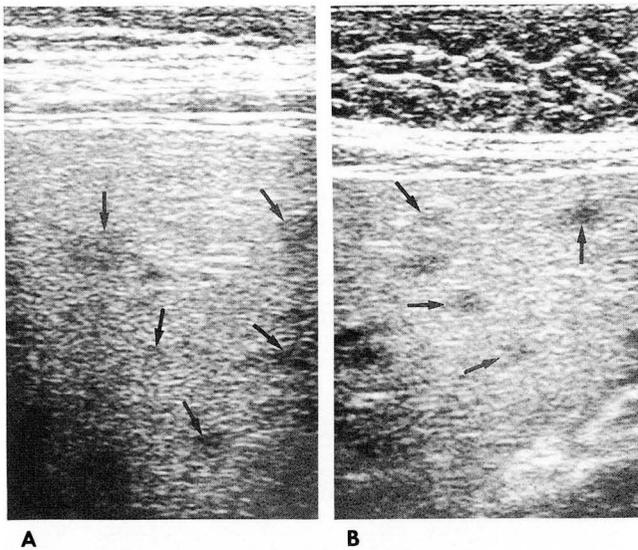


Fig. 8. Hepatosplenic candidiasis. A 13 year-old boy was under chemotherapy for Burkitt lymphoma of the colon. Sonography of the liver (**A**) and spleen (**B**) show numerous small hypoechoic nodules suggesting abscesses(arrow-s). Liver biopsy confirmed neutrophilic abscess with candida hyphae.

Neurotoxicity

Leukoencephalopathy includes acute or delayed changes in white matter, secondary to chemotherapy and/or radiation(7). Chemotherapeutic agents known to cause leukoencephalopathy include methotrexate, cisplatin, cytarabine, and thiotepea; it can also be caused by either intrathecal or high-dose intravenous

methotrexate. On T2-weighted MR images, diffuse and symmetric hyperintensities are seen in bilateral deep and periventricular white matter, with relative sparing of the cortex and subcortical U fibers(Fig. 6).

Cyclosporine is a common immunosuppressant used to prevent transplant rejection. It produces an encephalopathy accompanied by the following symptoms: seizures, cortical blindness, confusion, speech and motor derangements, and coma(8). The symptoms are dose dependent, and in many instances are reversible. Cyclosporine-induced neurotoxicity may be related to hypertensive encephalopathy, in which edema, predominantly in the subcortical white matter of the occipital, posterior temporal, and parietal lobes, is seen. MR demonstrates high signal intensity on T2-weighted images of the posterior regions of the brain, and on followup study, interval improvement is seen (Fig. 7).

Opportunistic Infections

All chemotherapeutic agents can produce myelosuppression and pancytopenia. Granulocytopenia poses the risk of life-threatening infections and fungal infections caused by candida and aspergillus species are common in neutropenic, immunosuppressed patients(1). Other opportunistic organisms such as pneumocystis carinii, or viruses-the pathogenicity of which is normally low- can produce serious disease. Hepatic and splenic microabscesses may accompany candida or mycobacterium infection(Fig. 8).

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소아에서 화학요법과 관련된 질병의 방사선 소견¹

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종양세포에만 선택적으로 작용하는 항암제는 적으며 정상세포 조직에의 독성 효과가 항상 문제가 된다. 소아의 악성종양에 대한 화학요법에 사용되는 항암제는 많은 종류가 있는데 bleomycin, doxorubicin, cyclophosphamide, L-asparaginase가 각각 폐섬유화, 심근 손상, 출혈성 방광염, 췌장염을 일으키는 것으로 잘 알려져 있다. 본 임상화보의 목적은 항암 화학요법과 관련되어 각종 장기에 나타나는 질병들의 방사선 소견을 알아보고자 하였다.

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